CLAIMS OBJECTIONS

Many claims stand objected to because of the use of the term "alfa". Claims 5,10-20, 18 and 36 stand objected to because for use of the term "BIW" in claims 10-20 and for errors of a typographical nature in claims 5, 18 and 36.

The Applicants have stated hereinabove the term "alfa" is a commonly used term understood by those skilled in the art to which the invention pertains. No correction is deemed necessary regarding use of the term "alfa" in reference to interferon.

Claim 36 have been renumbered as claim 37. Claims 5 and 18 have been amended to correct obvious typographical errors. Applicants thank the Examiner for bringing these errors to their attention.

Claims 10-20 are objected to for use of abbreviation "BIW".

Applicants are amending claim 10 to spell out the meaning of "BIW", thereby eliminating any possible confusion as to the meaning of this term in claims 10-20.

No change in scope, or new matter will be made and no new search will be required by entry of these amendments.

Reconsideration and withdrawal of these objections to the claims and specification are urged.

DOUBLE PATENTING

Claims 1-36 stand provisionally rejected under 35 U.S.C.§101 as claiming the same invention as that in the co-pending, commonly-owned U.S. Patent Application, Serial No. 09/311,487.

Applicants disagree that the claims in this application claim the same invention as that in co-pending, commonly-owned SN 09/311,487.

Reconsideration and withdrawal of this ground of rejection are urged.

OBVIOUS-TYPE DOUBLE PATENTING REJECTION

Claims 1-36 stand provisionally rejected under the judicially-created obviousness-type double patenting doctrine as being unpatentable over claims 1-43 of co-pending, commonly owned U.S. Patent Application Serial No. 09/464,425.

Applicants disagree that the instantly claimed subject matter is made obvious by that in co-pending commonly-owned SN 09/464,425. Applicants also assert that this rejection is premature and should be deferred until patentable subject matter is identified in each application.

Reconsideration and withdrawal of this ground of rejection are urged.

CLAIM REJECTION – 35 U.S.C. §112

Claims 1-36 stand rejected under 35 U.S.C.§112, second paragraph for being indefinite in that the phrase "a therapeutically effective induction dosing amount of interferon-alfa" in claim 1 is indefinite.

Applicants disagree. The term "therapeutically effective induction dosing" refers to higher doses of pegylated interferon-alfa, administered on a twice a week basis. These higher doses of pegylated interferon alfa are sufficient to lower detectable HCV-RNA serum levels-compared to the initial serum levels-in the early stage of the first treatment time period rather than administering lower doses of interferon or pegylated interferon alfa as taught in the prior art on a three-times a week, or once a week schedule. See, for example, the specification, on page 4, lines 9-31; page 5, lines 9-12,18-20, and 26-31; page 7, lines 2-5,11-15, and 21-24 for induction dosing amounts and induction dosing regimens for the various pegylated interferon-alfa for use in accordance with the present invention. Applicants' claimed invention is directed to method of more aggressively treating HCV infection than taught in the prior art by administering higher doses of interferon alfa on a daily basis in combination with the highest possible ribavirin doses on a daily basis to more quickly lower the detectable HCV-RNA levels. Applicants assert one skilled in the art would understand applicants' specification and claims.

Reconsideration and withdrawal of this ground of rejection are urged.

Claims 27-3 stand rejected under 35 USC§112, first paragraph for lack of enablement. It is asserted that the specification provides enablement for administering pegylated interferon alfa 2 or 3 times a week, but not once a week. Applicants disagree and assert that the specification enables one skilled in the art to practice the invention as claimed.

Schering has reported analysis of a pivotal Phase III study with 1.5 mcg per kg. of pegylated interferon alfa 2b once weekly and ribavirin (daily) in previously untreated (naive) adult patients with chronic hepatitis C to achieve a 61 percent rated of sustained vivologic response.

Reconsideration and withdrawal of this ground of rejection are urged.

CLAIM REJECTION – 35 U.S.C.§103(a)

Claims 1-37 stand rejected under 35 U.S.C.§(a) as being unpatentable over Chemello, et al., Grint, et al., and Gilbert, et al.

Chemello et al. discloses administering 15mg/kg of ribavirin and 3MIU of interferon alfa, TIW to a pilot group of HCV patients for six months. Nowhere does Chemello et al. discloses or suggests increasing the natural interferon alfa dose replacing natural interferon alfa with pegylated interferon alfa, much less administering higher doses daily of same, for extended periods of time, nor teach that such induction dosing would be safe or effective in knocking down the HCV-RNA viral load.

None of these deficiencies are cured by or Grint, et al.

Grint, et al. disclose a low dose of each of the drugs in combination therapy to reduce the side effects associated with administration of ribavirin and alfa interferon. See, Grint, et al. at page 3, line 19 to page 4, line 6 (or Grint, et al., col. 2, line 40 to column 5, line 11). Use of doses of 500 to no more than 800 mg of ribavirin and of doses of less than 3 million international units of interferon alfa- preferable 1 to no more than 2 million international units are taught. These doses are below the effective amounts of each drug taught and claimed by Applicants to be the "effective amount".

Moreover, Grint, et al. is directed to lower doses of each drug in the combination therapy to lower the side effects associated with the approved (higher) doses of interferon alfa and ribavirin. No motivation is thus provided to increase the amount of interferon as Applicants have discovered and claimed.

None of the deficiencies of Chemello, et al and/or Grint, et al. are cured by Gilbert, et al. which discloses alfa interferon conjugates are useful to treat many disease states. The statement, in Gilbert, et al., on page 12, lines 1-7 that "the conjugate is administered in amounts ranging from about 100,000 to about several million IU/m^2 depending, based on the mammal's condition" is no more than an invitation to experiment. There is no direction to enable one skilled in the art to make the many modifications in dosing and dosing regimen much less combine pegylated interferon alfa with a specific drug, ribavirin, to treat a specific disease, HCV.

Applicant also disagrees that there is any motivation provided in these disclosures to make the modification needed to bridge the gap to Applicant's claimed invention. Chemello et al, tells us to administer 15mg/kg of ribavirin and 3 MIU of interferon alfa, TIW for six months; Grint, et al. tell us to use less than an effective amount of each drug in the combination therapy for longer periods of time. Gilbert, et al provides a shotgun disclosure that is no more than an invitation to experiment. These disclosures teach away from Applicant's claimed invention.

Reconsideration and withdrawal of this ground of rejection are urged.

Reconsideration and withdrawal of this ground of rejection are urged.

Applicants assert that nowhere in any of these three references is there any teaching or suggestion to sue doses of pegylated interferon alfa greater than 3 MIU TIW.

Reconsideration and withdrawal of this ground of rejection are urged.

The marked up version of the Claims 5, 10 and 36 showing the amendments are attached as Appendix I

If Applicants can be of any assistance in advancing prosecution, please call the undersigned attorney of record.

Respectfully submitted,
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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to Assistant Commissioner for Patents, Washington, D.C. 20231, on

June 18, 2001

Thomas D. Hoffman
Registered Representative

Signature

6/18/2001
Date

APPENDIX I

Claim V rsion With Markings To Show Amendm nts

5.(amended) The method of claim 1, wherein the amount of ribavirin administered in the second treatment period is from about [aboujt]800 to 1200 mg per day.

10.(amended) The method of claim 1, wherein the pegylated interferon-alfa administered is pegylated interferon alfa-2b, and wherein the induction dosing amount of pegylated interferon alfa-2b administered in the first treatment time period is in the range of 0.5 to 1.5 micrograms per kilogram twice a week ("BIW")[BIW] for at least four weeks, and the amount of pegylated interferon alfa-2b administered in the second treatment time period is in the range of 0.5 to 1.5 micrograms per kilogram per week for up to forty-four weeks.

37.[36](amended) The method of claim 27, wherein the amount of ribavirin administered in the first and second treatment time periods is from about 800 to 1200 mg per day.